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EXAMINER	
SWITZER, JULIET CAROLINE	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/601,518	LIEW, CHOONG-CHIN	
	Examiner	Art Unit	
	Juliet C. Switzer	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17,19-21,23,24,28,29,31,33,34,38,41,43,49,56 and 59-63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17,19-21,23,24,28,29,31,33,34,38,41,43,49,56 and 59-63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/20/08 has been entered.

2. Claims 17, 19-21, 23-24, 28-29, 31, 33-34, 38, 41, 43, 49, 56, and 59-63 are pending. Applicant's amendments and arguments have been thoroughly reviewed, but are not sufficient to place the claims in condition for allowance for the reasons set forth in this office action. Any rejections not reiterated in this action have been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Priority

3. The claims have basis in parent applications 10/268730 and 09/477148, and thus have an effective filing date of at least 1/4/00.

4. The examiner was not able to identify basis in the provisional application 60/115,125 for the instantly claimed invention. For example, basis for the limitation that the blood samples have not been fractionated into cell types from subjects was not identified, nor basis for the current claims which recite analysis for each gene in a collection of two or more genes for the same disease, nor for quantifying a level of differential expression, nor for quantifying levels of RNA in samples. If applicant desires priority to the provisional application for the pending

claims, applicant should provide description of how each element of the pending claims is supported by the disclosure of the provisional application.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. The previously set forth rejection for NEW MATTER has been overcome by cancellation of claims 57 and 58 and amendment of the remaining claims to remove their dependency from claims 57 and 58.

Claim Rejections - 35 USC § 102

7. The rejection of claims 17, 19-21, 23-24, 28-29, 31, 33-34, 38, 41, 49, 56, 57, 58, and 61 are rejected under 35 U.S.C. 102(b) and 102(a) as being anticipated by Ralph et al. (WO 98/24935) or Ralph et al. (6190857) is WITHDRAWN. Applicant's arguments set forth 6/20/08 are persuasive, in part. Namely, the arguments are persuasive to establish that the phrase "total RNA from peripheral blood" does not have an unambiguous meaning in view of the cited prior art, in particular in view of Yu et al. discussed on page 9 of the remarks.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 17, 19, 20, 21, 23, 24, 28, 29, 31, 33, 34, 38, 41, 43, 49, 56, 61, 62, and 63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sharma et al. in view of Ralph et al. (WO 98/24935) or Ralph et al. (6190857).

Sharma et al. teach that from the very early stages of diseases the whole organism response to the changed condition (p. 10, 4th full ¶). In light of this, Sharma et al. teach a method for identifying a marker useful for diagnosing a disease comprising the steps of detecting the presence of RNA in an unfractionated sample of whole blood from each of one or more subjects having said disease and quantifying a level of said RNA in said sample. Namely, Sharma et al. teach the preparation of gene transcript patterns beginning with extraction of mRNA from tissues, cells or body parts of an individual or organism which has a disease or condition (p. 7, final ¶, p. 12, 1st ¶), and particularly teach the isolation of mRNA from blood samples which have not been fractionated into cell types (p. 35, section 5.1.1). Furthermore, the whole blood samples would contain RNA from leukocytes which have not been fractionated into cell types. Sharma et al. teach quantifying the level of expression and determining a difference between the quantified level in the sample from the diseased subject and a similarly quantified level of genes of control RNA from an unfractionated sample of whole blood from each of one or more first control subjects (p. 5, step (d); p. 15, first full ¶; p. 18, step (f); p. 11, final ¶). Sharma et al. teach that these methods are carried out by producing amplification products from RNA extracted from an unfractionated sample of whole blood (p. 18 and p. 35, Example 5).

Sharma et al. teach that the invention can detect diseases years before other subjective or objective symptoms may appear (p. 11, third full ¶).

Sharma et al. teach that diagnostic patterns can be provided that include markers of disease progression (p. 7, first ¶).

Sharma et al. teach the detection of many genes, including second, third, etc. (p. 16) genes and teach the sampling of more than one diseased and/or control subject to determine quantified levels of expressed markers (p. 21, first full ¶).

Sharma et al. teach detecting RNA by detecting cDNA derived from RNA (p. 18, steps (c) and (d), for example).

Sharma et al. teach quantifying the level of control RNA in said sample (p. 5, step (d); p. 15, first full ¶; p. 18, step (f); p. 11, final ¶). Sharma et al. teach isolating the control RNA into bands on an electrophoresis gel for quantification (p. 13).

Sharma et al. teach isolating RNA via extraction prior to the detection step (p. 12).

Sharma et al. teach that the subjects include human subjects (p. 7, 2nd full ¶).

Sharma et al. teach that control subjects should be free of disease (p. 9, first full ¶).

Sharma et al. teach that transcripts which exhibit altered expression at one or more stages of disease and which can be used together to provide a characteristic pattern which is indicative of a particular stage of disease can be identified (p. 7).

Sharma et al. that the methods of their invention are applicable to a wide variety of diseases and conditions, and teach that a disease in which their method would be useful is cancer of the bowel (p. 6-7).

Sharma et al. teach that their methods will result in the selection of between 2 and 1000 probe species for isolation, and that these probes reflect genes which have altered expression in the diseases or conditions in question, or particular stages thereof (p. 16, beginning at line 8).

Sharma et al. teach that known techniques of isolation of mRNA, construction and amplification of cDNA and selection through differential hybridization and differential display may be used to identify markers for the diagnostic probe patterns (¶ bridging pages 4-5).

Sharma et al. do not teach using an oligonucleotide of predetermined sequence or more specifically, primers specific for only RNA and/or cDNA complementary to said RNA, nor do they explicitly teach that the genes isolated are predominantly expressed in said non-blood tissue.

Ralph et al. carry out a very similar differential display method to identify markers of disease in blood and then confirm the differential expression using RT-PCR. Namely, Ralph et al. teach that responses secondary to disease states may be reflected in changing patterns of leukocyte mRNA levels that correlate with the presence of the disease state (Col. 5, lines 27-33). Throughout, Ralph et al. teach a method of identifying differentially expressed markers using RNA fingerprinting, and the techniques used by Ralph et al. include amplification of mRNA using random primers and identifying differentially expressed molecules using gel electrophoresis. Ralph et al. further explicitly teach that "frequently mRNAs identified by RNA fingerprinting or differential display as being differentially regulated turn out not to be so when examined by independent means. It is, therefore, critical that the differential expression of all mRNAs identified by RNA fingerprinting be confirmed as such by an independent methodology (paragraph bridging Col. 98-100)."

Ralph et al. exemplify this confirmation method in Example 5.6.2, beginning in column 98. Ralph et al. teach the use of RT-PCR to identify two or more markers useful for diagnosing a disease, namely prostate or breast cancer, exemplifying this method for the detection of two

transcripts referred to by Ralph et al. as UC331 and UC332, these sequences are RNA encoded by each of two genes (Example 5.6.2 and following, Col. 98).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the methods taught by Sharma et al. so as to have included the RT-PCR step using oligonucleotides of predetermined sequence as taught by Ralph et al. so as to have provided a means to confirm the differential expression of the identified markers within a complete method of identifying two or more markers useful for diagnosing a disease. Regarding the requirement that the subject genes are genes that are expressed in blood and non-blood tissue of a subject not having said disease, this is considered to be an inherent property of at least some of the genes that would be detected by the methods taught by Sharma et al. in view of Ralph et al. This is also true of the limitation of claim 61 which requires that the markers are predominately expressed in non-blood tissues. Sharma et al. in view of Ralph et al. are using substantially the same method steps as claimed by applicant, and so the detected transcripts would be expected to include genes expressed in blood and non-blood tissue of a subject not having said disease, as well as genes which are predominately expressed in non-blood tissues. Regarding claim 62, the specification does not define what is meant by a "candidate" marker. The genes which would be selected for follow-up analysis by amplification in the methods taught by Sharma et al. in view of Ralph et al. are considered "candidate" marker genes. Further, regarding claim 63, When the methods of Sharma et al. in view of Ralph et al. are applied to many of the diseases suggested by Sharma et al. (for example Alzheimer's disease) it is expected that some of the identified markers would be non-cancer-associated genes.

10. Claims 17, 20, 23, 28-29, 33-34, 41, 43, 49, and 59-63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sharma et al. in view of Lockhart et al. (Nature Biotechnology, Volume 14, December 1996).

The teachings of Sharma et al. as they relate to the instant claims have been previously set forth.

Sharma et al. do not teach using an oligonucleotide of predetermined sequence or more specifically, primers specific for only RNA and/or cDNA complementary to said RNA, nor do they explicitly teach that the genes isolated are predominantly expressed in said non-blood tissue.

Lockhart et al. describe a method for the simultaneous monitoring of many genes in parallel, and teach that in contrast to differential display methods, their methods are quantitative and allow the identification of the identity differentially expressed molecules quickly and easily. The method of Lockhart et al. uses microarrays. Lockhart et al. teach that because of the combinatorial nature of the chemistry involved and the ability to synthesize small arrays, their method is readily scalable to the monitoring of tens of thousands of genes. Lockhart et al. suggest that the quantitative monitoring of expression levels for large numbers of genes should prove valuable for a variety of uses, including identifying potential diagnostic targets.

Because both Sharma et al. and Lockhart et al. teach methods of analyzing differential expression of many genes from a single sample, it would have been obvious to one skilled in the art to substitute the microarray methods taught by Lockhart et al. for the differential display methods used by Sharma et al. to achieve the predictable result of identifying differentially expressed genes in the blood samples of Sharma et al. Further, one would have been motivated to make such a combination by the express teaching of Sharma et al. that known

techniques of isolation of mRNA, construction and amplification of cDNA and selection through differential hybridization and differential display may be used to identify markers for the diagnostic probe patterns (¶ bridging pages 4-5), and in order to take advantage of the benefits of differential hybridization using the microarrays taught by Lockhart et al. Regarding the requirement that the subject genes are genes that are expressed in blood and non-blood tissue of a subject not having said disease, this is considered to be an inherent property of at least some of the genes that would be detected by the methods taught by Sharma et al. in view of Lockhart et al. This is also true of the limitation of claim 61 which requires that the markers are predominately expressed in non-blood tissues. Sharma et al. in view of Lockhart et al. are using substantially the same method steps as claimed by applicant, and so the detected transcripts would be expected to include genes expressed in blood and non-blood tissue of a subject not having said disease, as well as genes which are predominately expressed in non-blood tissues. Regarding claim 62, the specification does not define what is meant by a "candidate" marker. Each of the genes which are analyzed using the microarrays taught by Lockhart et al. in the methods taught by Sharma et al. in view of Lockhart et al. are considered "candidate" marker genes. Further, regarding claim 63, When the methods of Sharma et al. in view of Lockhart et al. are applied to many of the diseases suggested by Sharma et al. (for example Alzheimer's disease) it is expected that some of the identified markers would be non-cancer-associated genes.

11. Claim 59 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sharma et al. in view of either Ralph et al. as applied to claims 17 and 19 above, and further in view of Wei et al. (Chinese Medical Journal, Volume 106(12):893-897, 1993).

12. Claim 59 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sharma et al. in view of Lockhart et al. as applied to claim 17 above, and further in view of Wei et al. (Chinese Medical Journal, Volume 106(12):893-897, 1993).

The teachings of Sharma et al. in view of Ralph et al. as they apply to claims 17 and 19 are previously discussed in this office action.

Likewise, the teaching of Sharma et al. in view of Lockhart et al. as they apply to claim 17 are previously discussed in this office action.

Sharma et al. teach that "the disease or condition may be any condition, ailment, disease or reaction that leads to the relative increase or decrease in the activity of informative genes… (p. 6, line 1)" and further teach a wide variety of diseases and conditions of various etiologies that are appropriate for the practice of their methods. Further, Ralph et al. teach that their method relies upon detecting a response of circulating leukocytes to the disease state (Col. 5, line 1) and that the detection of an immune response may be reflected in changing patterns of leukocyte mRNA levels that correlate with the presence of the disease state (Col. 5, 27-34).

Neither Sharma et al., Ralph et al., nor Lockhart et al. teach using their methods for the detection of markers for diabetes, in particular.

Wei et al. teach that insulin dependent diabetes mellitus is a kind of autoimmune disease, and furthermore teach that IL-6 is differentially expressed in the blood of patients having diabetes versus control patients. Thus, Wei et al. exemplify that at least a single differentially expressed molecule is present in the blood of patients having diabetes relative to healthy patients.

Therefore, at the time the invention was made, it would have been prima facie obvious to one of ordinary skill in the art to have applied the methods taught by Sharma et al. in view of

Ralph et al. or the methods taught by Sharma et al. in view of Lockhart et al. to the disease diabetes in order to identify additional markers in the blood that would be useful for detecting and understanding this disease. One would have been generally motivated by the teachings of Sharma et al. concerning the broad applicability of their methods, and by the teachings of Wei et al. that at least one marker differentially expressed in the blood of patients having diabetes versus healthy patients had been found.

Given the teachings of Sharma et al. and Ralph et al. one would have reasonably expected to identify numerous additional markers in RNA extracted from whole blood of the relevant subjects using differential display methods, and then to have confirmed those markers using the RT-PCR methods taught by Ralph et al. Likewise, given the teachings of Sharma et al. alone, one would have reasonably expected to identify numerous additional markers in RNA extracted from whole blood of the relevant subjects using the microarray methods taught by Lockhart et al.

Therefore, in view of the teachings of the prior art, the claimed invention is prima facie obvious.

13. Claim 60 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sharma et al. in view of either Ralph et al. as applied to claims 17 and 19 above, and further in view of Kasuga et al. (US 6133502).

14. Claim 59 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sharma et al. in view of Lockhart et al. as applied to claim 17 above, and further in view of Kasuga et al. (US 6133502).

The teachings of Sharma et al. in view of Ralph et al. as they apply to claims 17 and 19 are previously discussed in this office action.

Likewise, the teaching of Sharma et al. in view of Lockhart et al. as they apply to claim 17 are previously discussed in this office action.

Sharma et al. teach that "the disease or condition may be any condition, ailment, disease or reaction that leads to the relative increase or decrease in the activity of informative genes… (p. 6, line 1)" and further teach a wide variety of diseases and conditions of various etiologies that are appropriate for the practice of their methods. Further, Ralph et al. teach that their method relies upon detecting a response of circulating leukocytes to the disease state (Col. 5, line 1) and that the detection of an immune response may be reflected in changing patterns of leukocyte mRNA levels that correlate with the presence of the disease state (Col. 5, 27-34).

Neither Sharma et al. nor Ralph et al. teach using their methods for the detection of markers for heart failure, in particular.

Kasuga et al. teach that expression of monocyte chemotactic and activating factor mRNA is known to increase in the blood of acute heart failure patients.

Therefore, at the time the invention was made, it would have been prima facie obvious to one of ordinary skill in the art to have applied the methods taught by Sharma et al. in view of Ralph et al. to the disease heart failure in order to identify additional markers in the blood that would be useful for detecting and understanding this disease. One would have been generally motivated by the teachings of Sharma et al. (and Ralph et al.) concerning the broad applicability of their methods, and by the teachings of Kasuga et al. that at least one marker differentially expressed in the blood of patients having heart failure versus healthy patients had been found.

Given the teachings of Sharma et al. and Ralph et al. one would have reasonably expected to identify numerous additional markers in RNA extracted from whole blood of the relevant subjects using differential display methods, and then to have confirmed those markers using the RT-PCR methods taught by Ralph et al. Likewise, given the teachings of Sharma et al. alone, one would have reasonably expected to identify numerous additional markers in RNA extracted from whole blood of the relevant subjects using the microarray methods taught by Lockhart et al. Therefore, in view of the teachings of the prior art, the claimed invention is prima facie obvious.

Double Patenting

15. The previously set forth rejections for obviousness type double patenting are maintained and applied to newly added claims 62-63. Applicant did not provide any arguments particularly traversing these rejections.

Response to Remarks

Applicant traverses a previously set forth rejection over Ralph et al. in view of Sharma et al. (beginning on page 16 of the Response). Applicant points out that Ralph et al. first uses promiscuous probes, which is in direct contrast to the limitation of the instant claims which require the use of a probe which is specific for the biomarker. However, Ralph et al., and indeed the instant rejection of Sharma et al. in view of Ralph et al. also teaches the use of methods which use gene specific primers, oligonucleotides specific for a biomarker. The fact that the methods of the prior art use two different methods in serial to identify biomarkers does not distinguish them from the claimed method. The claimed methods are drawn using "comprising"

language, and so, when the structural method limitations are met by the teachings of the prior art, additional steps are also permitted to be included in the methods of the prior art.

Applicant points out that Ralph et al. do not use the proper RNA sample as set forth in the instant claims. This deficiency is cured by the primary reference, Sharma et al.

Applicant traverses a rejection set forth over Sharma et al. in view of Ralph et al. beginning on page 17 of the Response. Applicant reiterates the argument that the method of Sharma et al. in view of Ralph et al. uses a method of identifying markers which first employs promiscuous probes, and then follows up with gene specific amplification. Applicant's argument appears to be that because Sharma et al. in view of Ralph et al. use gene specific primers to confirm the differential expression of a transcript that was previously identified by differential display, the gene specific amplification portion of the assay is not part of the method for identifying markers. This argument is not persuasive because the totality of the method taught by Sharma et al. in view of Ralph et al. is in its entirely directed towards eventually identifying markers. This method uses a two step procedure to make such an identification. As noted previously, the instant claims are drawn using comprising language, and so, do not exclude a method wherein markers are "identified" using a two step process of differential display followed by amplification. Applicant's attempts to construe the Ralph et al. method as two distinct methods fails to acknowledge the point that Ralph et al. teaches that since differential display methods are often false confirmation is necessary. Confirmation must occur before one can actually conclude that a differentially expressed marker has been identified. Prior to that, the transcripts identified by differential display are "candidate" markers. The structural method steps are met by the teachings of the prior art, and so, applicant's arguments are not persuasive.

Also, it is noted that applicant is attempting to distinguish their methods from that of the prior art based on the preamble of the claims. In this case the preamble sets forth the intended use of the method, it does not structurally limit the method steps. Again, as previously stated, the method set forth in the prior art teaches all of the structural limitations of the claimed invention.

Applicant traverses the rejection of claim 59, beginning on page 19 of the response. Applicant reiterates the supposed deficiencies of Sharma et al. in view of Ralph et al. which have been previously addressed.

Further, applicant points out that Wei et al. is silent with respect to the differential expression of a second RNA molecule in the peripheral blood mononuclear cells of patients with IDDM, and so, applicant contends that there would not have been reasonable expectation of success. However, this ignores Sharma et al. specific teachings that from the very early stages of diseases the whole organism response to the changed condition, and as a result panels of differentially expressed molecules can be identified. Applicant's assertion of no expectation of success is an attorney argument which is not supported by the evidence on the record. Applicant states that none of the references provide one of skill at the time of the invention a scientific basis for a reasonable expectation of success. However, the fact that the Ralph et al. and Sharma et al. are considered skilled in their fields and that they set forth their teachings very clearly enjoys a presumption that they are valid. There is no evidence on the record to suggest that their teachings are not valid.

Applicant again attempts to distinguish the claimed methods from "an independent method of confirming a marker already identified." This argument has previously been

addressed. Again, it is reiterated that applicant's instant claims are drawn using open comprising language, and as such allow for additional steps. The fact that the instant claims sets forth an RT-PCR step as step (a) does not exclude methods where additional steps occur prior to the RT-PCR step.

Applicant traverses the rejection of claim 60 on beginning on page 21 of the response. Applicant's remarks are duplicative of those that have been previously addressed. The rejection is maintained.

Previous discussion on the record of this application relates to an assertion that Sharma et al. teach away from using "sequence based methods." However, upon further consideration, the examiner WITHDRAWS this position, namely in view of Sharma's teaching that differential hybridization methods can be used to identify differentially expressed markers. The examiner was not aware of this particular teaching in the Sharma et al. disclosure when the previous statements were made. Any inconvenience is regretted.

Conclusion

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C Switzer whose telephone number is (571) 272-0753. The examiner can normally be reached on Tuesday and Wednesday, from 10:00 AM until 5:00 PM, and on Friday from 12:30 PM until 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached by calling (571) 272-0735.

The fax phone numbers for the organization where this application or proceeding is assigned are (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-0507.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Juliet C. Switzer/
Primary Examiner
Art Unit 1634

September 16, 2008